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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,412	10/22/2003	Evangelia G. Kranias	10738-47	2386

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EXAMINER	
SITTON, JEHANNE SOUAYA	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,412	KRANIAS ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-14,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 October 2003* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, claim 15 in the reply filed on 11/9/2005 is acknowledged. The traversal is on the ground(s) that it would not be unduly burdensome for the examiner to examine all of the claims since the independent claims all require comparisons and analysis with respect to a nucleotide fragment with a predetermined phospholamban nucleotide sequence fragment. This is not found persuasive because the claims are not limited to any specific sequence nor to analysis of human phospholamban. Accordingly, the search for mutant sequences of SEQ ID NO: 1 are not coextensive with the search for claims 1-14 and 16-17, which do not recite any particular sequence. Secondly, the search for the structural components of a product, in this case a mutant nucleic acid fragment comprising SEQ ID NO: 1, would not necessarily provide any information regarding disease susceptibility in any species. Accordingly, a search burden does exist for searching both patentably distinct groups.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The disclosure is objected to because of the following: Figure 3 contains panel A and B, however, in the "Detailed Description of the Drawings" section of the specification, the description does not provide for an explanation of both panels. Appropriate correction is required, however applicants should take care not to introduce new matter into the disclosure.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim appears to encompass any nucleic acid comprising SEQ ID NO: 1, but which is polymorphic with respect to SEQ ID NO: 1 or polymorphic on either side of SEQ ID NO: 1, from any source, as well as polymorphic fragments of SEQ ID NO: 1. The claims therefore encompass an extremely large genus of nucleic acid variants, homologs, and mutants of SEQ ID NO: 1, from any source. The specification, however, has only described a single polymorphism within SEQ ID NO: 1, T to G at position 116, which is associated with dilated cardiomyopathy (DCM) when present as a homozygous mutation (see pages 10-11 and 16 of the specification). SEQ ID NO: 1 appears to encode the full length 52 amino acid human phospholamban protein. The claim encompasses a large genus of nucleic acids which comprise polymorphisms at any position of SEQ ID NO: 1 or anywhere in genomic sequences on either side of SEQ ID NO: 1. The genus includes an enormous number of polymorphisms for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named polymorphism for which data is provided demonstrating an association in homozygous form with DCM. Thus, applicant has express possession of only 1 particular

polymorphism, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed which would permit selection of sequences as polymorphisms. No written description of alleles, of upstream or downstream regions containing additional sequence, which are mutated or associated with DCM are described in the specification. The single T to C polymorphism at position 116 within SEQ ID NO: 1 is not representative of the large genus of mutants and variants of SEQ ID NO: 1 or homologs of SEQ ID NO: 1 from any source. For example, Schmitt (Schmitt et al; Science, vol. 299, pages 1410-1413; 2003) teaches a C to T mutation at position 25 leading to an Arg to Cys mutation at amino acid 9, of human phospholamban. The instant specification provides no description or guidance as to the existence of this polymorphism. The instantly disclosed polymorphism leading to a stop codon at amino acid 39 does not appear to be representative of the polymorphism at position 9 taught by Schmitt because the polymorphism taught by Schmitt appears to be disease associated in the heterozygous state whereas the instantly disclosed polymorphism at position 116 only appears associated in the homozygous state (specification at page 16 teaches that individuals in the heterozygous state did not show any detectable clinical phenotype). Secondly, the instantly disclosed polymorphism results in a mutation in the transmembrane domain of phospholamban, whereas the mutation disclosed by Schmitt is in domain Ia. The teachings of the specification provide no way to predict the existence or affect of the polymorphism taught by Schmitt.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of

skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) In the instant case, the specification fails to teach the necessary common attributes or features of the genus of encompassed nucleic acids and polymorphisms in view of the species disclosed. As such, one of skill in the art would not recognize that applicant was in possession of the genus of nucleic acids and polymorphisms encompassed by the broadly claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids and polymorphisms, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The current situation is a definition of the compound solely based on its functional utility, as a polymorphism, without any definition of the particular polymorphisms claimed.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim recites "an isolated phospholamban polymorphism fragment *comprising* SEQ ID NO: 1". This recitation is confusing because the term "comprising" is normally taken to mean the full sequence of SEQ ID NO: 1 with any nucleotides on either side, however the context is unclear in this situation because the only mutation/polymorphism taught in the specification is at position 116 of SEQ ID NO: 1, wherein said position is a G instead of a T. However, SEQ ID NO: 1 appears to be drawn to the wildtype sequence (T at position 116), therefore it is not clear whether the term comprising is limited to the sequence of SEQ ID NO: 1, in this case does not have a polymorphism, or to a sequence comprising SEQ ID NO: 1 where

the polymorphism occurs in the nucleotides on either side of SEQ ID NO: 1, or to any mutation/polymorphism within SEQ ID NO: 1. Additionally, the term "fragment" is confusing because it is unclear if the term intends fragments from within SEQ ID NO: 1, (which, however, is contraverted by the term "comprising"), or whether the full sequence of SEQ ID NO: 1 is a fragment of a larger phospholamban nucleic acid. As SEQ ID NO: 1 appears to encode the full length 52 amino acid phospholamban protein, the metes and bounds of the term fragment are also unclear. The specification does not define the recitations of "fragment" and "comprising". The metes and bounds of the claim are therefore unclear.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession number X15075 (September 1993).

Accession number X15075 teaches the mRNA for pig phospholamban which is polymorphic with respect to SEQ ID NO: 1 at 10 positions (10 mismatches -see alignment). Given that neither the claim nor the specification provides any definition of "comprising" or "fragment" (see 112/2nd paragraph rejection above), the claim has been broadly interpreted to encompass a nucleic acid that has polymorphisms or mutations with respect to SEQ ID NO: 1. The term fragment does not distinguish the claimed nucleic acid from the teachings of Accession number X15075.

8. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession number M60411 (Jan 1995).

Accession number M60411 teaches the mRNA for human phospholamban which comprises SEQ ID NO: 1. The claim has been broadly interpreted to encompass a nucleic acid "comprising" SEQ ID NO: 1 (see 112/2nd paragraph rejection above).

9. Claim 15 is rejected under 35 U.S.C. 102(a) as being anticipated by Kimura (Kimura et al; Mol. Pharmacol, vol. 61, pages 667-673, 2002).

Kimura teaches constructing S16D and T17D mutants of human phospholamban DNA (see col. 2, page 668 "Oligonucleotide directed mutagenesis) from a fragment of the DNA encoding human phospholamban: Met-1 to Gln-26. Given that neither the claim nor the specification provides any definition of "comprising" or "fragment" (see 112/2nd paragraph rejection above), the claim has been broadly interpreted to encompass a nucleic acid which is a fragment of SEQ ID NO: 1 and which has polymorphisms with respect to SEQ ID NO: 1.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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1/10/06